PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference 4 -32997B/USN	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/EP2004/003656	International filing date *(day/month/year)* 06 April 2004 (06.04.2004)	Priority date *(day/month/year)* 08 April 2003 (08.04.2003)]
International Patent Classification (IPC) or national classification and IPC [7] A61K 9/20, 9/48		
Applicant NOVARTIS AG		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 14 October 2005 (14.10.2005)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	Authorized officer Agnes Wittmann-Regis Telephone No. +41 22 338 89 70

PATENT COOPERATION TREATY

RECEIVED
20 AUG 2004
WIPO PCT

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/003656	06.04.2004	08.04.2003

International Patent Classification (IPC) or both national classification and IPC
A61K9/20, A61K9/48

Applicant
NOVARTIS AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

VON EGGELKRAUT, S

Telephone No. +31 70 340-4732

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1,3,4
	No:	Claims	2,5-10
Inventive step (IS)	Yes:	Claims	2
	No:	Claims	1,3-10
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item V.

1 The following documents are referred to in this communication:
D1 : EP 1 002 792 A (YOSHITOMI PHARMACEUTICAL) 24 May 2000 (2000-05-24)
D2 : WO 02/18395 A (PARSONS WILLIAM H ; HAJDU RICHARD (US); BERGSTROM JAMES (US); CARD DEB) 7 March 2002 (2002-03-07)
D3 : EP 1 050 301 A (YOSHITOMI PHARMACEUTICAL) 8 November 2000 (2000-11-08)

2 INDEPENDENT CLAIM 1

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT.
Document D1 discloses (the references in parenthesis applying to this document): Solid compositions comprising a S1P receptor agonist. The compositions may comprise the sugar alcohols mannitol or maltitol. Routine additives such as magnesium stearate can also be added (page 19, lines 53-55, paragraph 184. 2-amino-2-(2-(4- (1-oxo-5- phenylpentyl) phenyl) ethyl) propane-1,3-diol is a preferred drug (paragraphs 241, 243, 258; claims 2). Tablets with the 1 mg of the compound, 90 mg lactose, 25 mg crystalline cellulose and 4 mg magnesium stearate are disclosed in paragraph 272.

2.2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not inventive in the sense of Article 33(3) PCT.
Document D2 discloses (the references in parenthesis applying to this document): Tablets and capsules comprising a S1P receptor agonist and excipients including magnesium stearate (page 18, lines 1-16).

3 DEPENDENT CLAIMS 3-10
Dependent claims 3-10 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step (Article 33(2) and (3) PCT).

4 DEPENDENT CLAIM 2

The combination of the features of dependent claim 2 is neither known from, nor rendered obvious by, the available prior art. The reasons are as follows:

Document D3 discloses liquid compositions for injection comprising 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol and mannitol.

Neither D3 nor D1 or D2 disclose or suggest a solid oral pharmaceutical composition comprising 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol or 2-amino-2- (2-(4- (1-oxo-5- phenylpentyl) phenyl) ethyl) propane-1,3-diol and a sugar alcohol.